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XARELTO® to be Studied with Factor Xa Inhibitor Antidote

Janssen and Bayer Announce Clinical Collaboration Agreement with Portola

RARITAN, N.J., Feb. 5, 2013 /PRNewswire/ -- Janssen Pharmaceuticals, Inc. (Janssen) today announced a clinical collaboration agreement with Portola Pharmaceuticals, Inc. and Bayer HealthCare to evaluate the safety of PRT4445 — an investigational-stage antidote for Factor Xa inhibitors — in healthy volunteers who have been administered the oral anticoagulant XARELTO® (rivaroxaban). The study will evaluate several dosage strengths of PRT4445 and its ability to reverse the anticoagulant activity of XARELTO® in emergency situations.

XARELTO® is approved by the U.S. Food and Drug Administration (FDA) for six distinct uses. This proof-of-concept study is scheduled to complete in the second half of 2013. A phase 3 trial will be required prior to submitting PRT4445 to the FDA for approval in this setting. Standard clinical measures are currently employed to manage these patients and events.

"XARELTO® has the broadest indication profile of any of the new oral anticoagulants in the U.S. market, and is being used by a wide array of patients in many different settings," said Larry E. Fields, M.D., Senior Director, Clinical Development, Medical Affairs at Janssen. "We are committed to exploring ways to expedite reversal of the drug's effects when necessary, which could provide physicians with an additional treatment option during emergency situations."

As part of the agreement, Janssen and Bayer will make an upfront payment to Portola and will provide development and regulatory guidance for the study. Portola retains full global development and commercialization rights for PRT4445.

To date, more than 2.5 million patients have received XARELTO® worldwide and more than one million prescriptions have been written in the U.S. XARELTO® is broadly reimbursed for more than 90% of commercial and Medicare health plan members, with the majority covered at the lowest branded co-pay.

Janssen Pharmaceuticals, Inc. holds U.S. marketing rights for XARELTO®, and is supported by the Bayer HealthCare U.S. sales force in designated hospital accounts.

About PRT4445
Portola Pharmaceutical's PRT4445 is a novel recombinant protein designed to reverse the anticoagulant activity in patients treated with Factor Xa inhibitors suffering from an uncontrolled bleeding episode or undergoing emergency surgery. It is similar to native Factor Xa but has structural modifications intended to restrict its biological activity to reverse the effects of Factor Xa inhibitors. PRT4445 works by binding Factor Xa inhibitors in the blood, thereby preventing them from inhibiting the activity of native Factor Xa. As a result, the native Factor Xa is available to participate in the coagulation process and restore normal clotting.

About XARELTO® (rivaroxaban)
XARELTO® is approved for six distinct uses:

1. To reduce the risk of blood clots in the legs and lungs of people who have just had knee replacement surgery.
2. To reduce the risk of blood clots in the legs and lungs of people who have just had hip replacement surgery.
3. To reduce the risk of both hemorrhagic and thrombotic strokes as well as other blood clots in people with atrial fibrillation not caused by a heart valve problem. There is limited information on how XARELTO® compares to a medicine called warfarin in reducing the risk of stroke when the effects of warfarin are well controlled.
4. To treat people with pulmonary embolism (PE).
5. To treat people with deep vein thrombosis (DVT).
6. To reduce the risk of recurrence of DVT or PE following an initial six months of treatment for acute venous thromboembolism.

There are two additional indications currently submitted and under review at the FDA.

XARELTO® works by blocking the blood clotting enzyme Factor Xa, and does not require routine blood monitoring. The

extensive program of clinical trials evaluating XARELTO® in more than 75,000 makes it the most studied oral, Factor Xa inhibitor in the world today.

Janssen Research & Development, LLC, and Bayer HealthCare together are developing rivaroxaban.

The XARELTO® CarePath™ Support Program is a resource designed for health care providers, patients and caregivers. Visit goxarelto.com or call 1-888-XARELTO to learn more about the XARELTO® CarePath™ resources focused on access, educatio and adherence.

Important Safety Information

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT XARELTO®?

- **For people taking XARELTO® for atrial fibrillation**:
  People with atrial fibrillation (an irregular heart beat) are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. XARELTO® lowers your chance of having a stroke by helping to prevent clots from forming. If you stop taking XARELTO®, you may have increased risk of forming a clot in your blood.
  Do not stop taking XARELTO® without talking to the doctor who prescribes it for you. Stopping XARELTO® increases your risk of having a stroke.
  If you have to stop taking XARELTO®, your doctor may prescribe another blood thinner medicine to prevent a blood clot from forming.
- XARELTO® can cause bleeding, which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner medicine that reduces blood clotting. While you take XARELTO® you are likely to bruise more easily and it may take longer for bleeding to stop

You may have a higher risk of bleeding if you take XARELTO® and take other medicines that increase your risk of bleeding, including:

- Aspirin or aspirin-containing products
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Warfarin sodium (Coumadin®, Jantoven®)
- Any medicine that contains heparin
- Clopidogrel (Plavix®)
- Other medicines to prevent or treat blood clots

Tell your doctor if you take any of these medicines. Ask your doctor or pharmacist if you are not sure if your medicine is one listed above.

Call your doctor or get medical help right away if you develop any of these signs or symptoms of bleeding:

- Unexpected bleeding or bleeding that lasts a long time such as:
  - Nosebleeds that happen often
  - Unusual bleeding from gums
  - Menstrual bleeding that is heavier than normal, or vaginal bleeding
- Bleeding that is severe or that you cannot control
- Red, pink, or brown urine
- Bright red or black stools (looks like tar)
- Cough up blood or blood clots
- Vomit blood or your vomit looks like "coffee grounds"
- Headaches, feeling dizzy or weak
- Pain, swelling, or new drainage at wound sites

Spinal or epidural blood clots (hematoma): People who take a blood thinner medicine (anticoagulant) like XARELTO®, and have medicine injected into their spinal and epidural area, or have a spinal puncture have a risk of forming a blood clot than can cause long-term or permanent loss of the ability to move (paralysis). Your risk of developing a spinal or epidural blood clot is higher if:

- a thin tube called an epidural catheter is placed in your back to give you certain medicine

- you take NSAIDs or a medicine to prevent blood from clotting
- you have a history of difficult or repeated epidural or spinal punctures
- you have a history of problems with your spine or have had surgery on your spine

If you take XARELTO® and receive spinal anesthesia or have a spinal puncture, your doctor should watch you closely for symptoms of spinal or epidural blood clots. Tell your doctor right away if you have tingling, numbness, or muscles weakness, especially in your legs and feet.

WHO SHOULD NOT TAKE XARELTO®?

Do not take XARELTO® if you:

- Currently have certain types of abnormal bleeding. Talk to your doctor before taking XARELTO® if you currently have unusual bleeding.
- Are allergic to rivaroxaban or any of the ingredients of XARELTO®.

WHAT SHOULD I TELL MY DOCTOR BEFORE OR WHILE TAKING XARELTO®?

Before taking XARELTO®, tell your doctor if you:

- Have ever had bleeding problems
- Have liver or kidney problems
- Have any other medical condition
- Are pregnant or plan to become pregnant. It is not known if XARELTO® will harm your unborn baby. Tell your doctor right away if you become pregnant while taking XARELTO®. If you take XARELTO® during pregnancy, tell your doctor right away if you have bleeding or symptoms of blood loss.
- Are breastfeeding or plan to breastfeed. It is not known if XARELTO® passes into your breast milk. You and your doctor should decide if you will take XARELTO® or breastfeed.

Tell all of your doctors and dentists that you are taking XARELTO®. They should talk to the doctor who prescribed XARELTO® for you before you have any surgery, medical or dental procedure.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO® works. Certain medicines may increase your risk of bleeding.

Especially tell your doctor if you take:

- Ketoconazole (Nizoral®)
- Itraconazole (Onmel™, Sporanox®)
- Ritonavir (Norvir®)
- Lopinavir/ritonavir (Kaletra®)
- Indinavir (Crixivan®)
- Carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol®-XR, Teril™, Epitol®)
- Phenytoin (Dilantin-125®, Dilantin®)
- Phenobarbital (Solfoton™)
- Rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®)
- St. John's wort (*Hypericum perforatum*)

Ask your doctor if you are not sure if your medicine is one listed above. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

HOW SHOULD I TAKE XARELTO®?

Take XARELTO® exactly as prescribed by your doctor. **Do not change your dose or stop taking XARELTO® unless your doctor tells you to.**

- Your doctor will decide how long you should take XARELTO®. Do not stop taking XARELTO® without talking with your doctor first.
- Your doctor may change your dose if needed,

For people who have:

- **Atrial Fibrillation:** Take XARELTO® 1 time a day with your evening meal. Stopping XARELTO® may increase your risk of having a stroke or forming blood clots in other parts of your body.
- **Blood clots in the veins of your legs or lungs:**
  - To treat blood clots, take XARELTO® once or twice a day according to your doctor's instructions. XARELTO® is usually taken with food. Take XARELTO® at the same time each day.
- **Hip or knee replacement surgery:** Take XARELTO® 1 time a day with or without food.

- Your doctor may stop XARELTO® for a short time before any surgery, medical or dental procedure. Your doctor will tell you when to start taking XARELTO® again after your surgery or procedure
- Do not run out of XARELTO®. Refill your prescription for XARELTO® before you run out. When leaving the hospital following a hip or knee replacement, be sure that you have XARELTO® available to avoid missing any doses.
- If you miss a dose of XARELTO®, take it as soon as you remember on the same day and continue with your next regularly scheduled dose.
- If you take too much XARELTO®, go to the nearest hospital emergency room or call your doctor right away.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

XARELTO® can cause bleeding, which can be serious, and rarely may lead to death. ***Please see "What is the most important information I should know about XARELTO®?"***

Tell your doctor if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You are also encouraged to report side effects to the FDA: visit *http://www.fda.gov/medwatch* **or call 1-800-FDA-1088.** You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).

Please click here for full prescribing information, **including Boxed Warnings** and the Medication Guide.

About Janssen Pharmaceuticals, Inc.
As a member of the Janssen Pharmaceutical Companies of Johnson & Johnson, Janssen Pharmaceuticals, Inc. is dedicated to addressing and resolving the major unmet medical needs of our time. Driven by our commitment to patients, healthcare professionals, and caregivers, we strive to develop sustainable and integrated healthcare solutions by working in partnership with all stakeholders on the basis of trust and transparency. Our daily work is guided by meeting goals of excellence in quality, innovation, safety, and efficacy in order to advance patient care.

Our company provides medicines for an array of health concerns in several therapeutic areas. Other innovative therapies that Janssen Pharmaceuticals, Inc. offers include ACIPHEX® (rabeprazole sodium), DORIBAX® (doripenem for injection), ELMIRON® (pentosan polysulfate sodium), NUCYNTA® (tapentadol) and NUCYNTA® ER (tapentadol extended-release tablets). The full prescribing information for NUCYNTA® and NUCYNTA® ER, including boxed warnings, are available here and here.

For more information on Janssen Pharmaceuticals, Inc., visit us at www.janssenpharmaceuticalsinc.com or follow us on Twitter at www.twitter.com/JanssenUSand on YouTube at www.Youtube.com/JanssenUS.

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceuticals, Inc., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to, general industry conditions and competition; economic factors, such as interest rate and currency exchange rate fluctuations; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory

approvals; challenges to patents; changes in behavior and spending patterns or financial distress of purchasers of healthcare products and services; changes to governmental laws and regulations and domestic and foreign health care reforms; trends toward health care cost containment; and increased scrutiny of the healthcare industry by government agencies. A further list and description of these risks, uncertainties and other factors can be found in Exhibit 99 of Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2012. Copies of this Form 10-K, as well as subsequent filings, are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. Neither Janssen Pharmaceuticals, Inc. nor Johnson & Johnson undertakes to update any forward-looking statements as a result of new information or future events or developments.)

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